IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PURDUE PHARMA PRODUCTS L.P., NAPP PHARMACEUTICAL GROUP LTD., BIOVAIL LABORATORIES INTERNATIONAL SRL, and ORTHO-MCNEIL, INC.,	)	
Plaintiffs,	)	C.A. No. 07-255-JJF (Consolidated)
v.	)	
PAR PHARMACEUTICAL, INC. and PAR PHARMACEUTICAL COMPANIES, INC.,	)	**NON-CONFIDENTIAL VERSION**
Defendants.	)	

DEFENDANTS' OPENING CLAIM CONSTRUCTION BRIEF

Of Counsel

Edgar H. Haug
Robert E. Colletti
Frommer Lawrence & Haug LLP
745 Fifth Avenue
New York, NY 10151
(212) 588-0800

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Frederick L. Cottrell, III (#2555)
Cottrell@rlf.com
Steven J. Fineman (#4025)
Fineman@rlf.com
Richards, Layton & Finger P.A.
One Rodney Square
P.O. Box 551
Wilmington, DE 19899
(302) 651-7700
Attorneys for Defendants Par Pharmaceutical, Inc. and Par Pharmaceutical Companies, Inc.

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I. INTRODUCTION

Defendants Par Pharmaceutical, Inc. and Par Pharmaceutical Companies, Inc. ("Par") submit this brief on claim construction for the '887 and the '430 patents.[1] (D.I. 23). These patents are generally directed to controlled release oral preparations of tramadol, an analgesic. The disputed claim terms — and Par's proposed definitions of them — are set forth below:

Disputed Claim Term	Par's Proposed Construction
"Therapeutic Effect"	The controlled release oral pharmaceutical preparation must produce analgesic efficacy in human patients experiencing pain as demonstrated by scientifically valid placebo-controlled clinical evidence.
"Therapeutic Effect For At Least About 24 Hours" and "Therapeutic Effect For About 24 Hours After Oral Administration"	The controlled release oral pharmaceutical preparation must produce analgesic efficacy in human patients experiencing pain as demonstrated by scientifically valid placebo-controlled clinical evidence and subsequent to oral administration of a dose of the preparation the analgesic efficacy in the patients must last for a period of about 24 hours from the time of onset of action.
"Matrix"	A system wherein a drug is incorporated into a polymer(s) structure by either particle or molecular dispersion, wherein the former is a suspension of drug particles homogenously distributed in the polymer(s) structure and in the latter drug molecules are dissolved in the polymer, and wherein drug release occurs by diffusion through and/or erosion of the polymer structure.
"Normal Release Matrix"	A matrix that does not slow the release of the active ingredient.
"Pharmaceutically Effective Amount of Tramadol Or a Salt Thereof"	An amount of tramadol or its salt contained in the substrate or the normal release matrix to achieve a therapeutic effect.

[1] U.S. Patent Nos. 6,254,887 ("the '887 patent") and 7,074,430 ("the '430 patent") (collectively, "the patents-in-suit").

Par's proposed claim constructions are based on the plain meaning of these terms supplied by the intrinsic record and by relevant extrinsic evidence, including technical textbooks, and the declaration of its expert, Dr. Michael L. Weinberger, who among other things serves as the Medical Director of the Pain Management Center; Division Chief, Pain Medicine Department of Anesthesiology; and Medical Director, Palliative Medicine Program at New York Presbyterian Hospital (Columbia University Medical Center).

II. NATURE AND STAGE OF THE PROCEEDING

Plaintiffs filed this action for infringement of the '887 and '430 patents against Par. (D.I. 78).[2] It is based on Par's submission to the U.S. Food and Drug Administration ("FDA"), pursuant to the Hatch-Waxman Act, of Abbreviated New Drug Application ("ANDA") No. 78-783 ("Par's ANDA"). Par's ANDA seeks FDA approval to market generic tramadol extended-release tablets. At issue in this case is whether the products described in Par's ANDA would, if marketed, infringe the '887 patent or the '430 patent, and whether these patents are valid and enforceable.

This case is currently in the expert phase of discovery, which is scheduled to be completed by August 15, 2008.[3] (D.I. 23). Claim construction is scheduled to be fully briefed by July 22, 2008. (D.I. 23). A Markman hearing has been scheduled for August 1, 2008.

[2] Plaintiffs are asserting claims 1, 3, 13, 15-16, 19, 23, 27, 29 and 31 of the '887 patent and claims 1, 3, 5-7 and 11-15 of the '430 patent.

[3] Although fact discovery was due to be completed on June 5, 2007, Par has moved to compel production of certain of certain discovery and amend the Scheduling Order. (D.I. 152-154).

III. SUMMARY OF ARGUMENT

A patent's claims serve an important public notice function and define the patentee's right to exclude. Disputed claim terms need to be construed so as to determine their legally operative meaning and scope. As set forth in detail below, Par's constructions are supported by the plain meaning of the claim language of the patents-in-suit, the written description, and the prosecution histories of the patents-in-suit, informed by and consistent with dictionaries, treatises and expert testimony on what a person of ordinary skill in the art at the time of invention would have understood.

IV. STATEMENT OF FACTS

Tramadol is an orally active analgesic that was discovered in the 1960's by Grünenthal GmbH and has been marketed in Germany since the 1970's. Plaintiff Ortho-McNeil, Inc. ("Ortho-McNeil") licensed rights to tramadol in the United States from Grünenthal GmbH in the 1980's and began selling immediate release tramadol hydrochloride tablets in the 1990's under the tradename Ultram®.

The '887 patent and the '430 patent are classic life-cycle management, "line extension" patents concerning controlled-release preparations of tramadol. Plaintiff Purdue Pharma Products L.P. ("Purdue") originally licensed the '887 patent to Ortho-McNeil. Purdue and Ortho-McNeil then unsuccessfully sought FDA approval for their own controlled-release tramadol product, Ultram® SR. After failing to obtain FDA-approval for Ultram® SR, Ortho-McNeil sublicensed Plaintiff Biovail Laboratories International SRL ("Biovail"), which holds New Drug Application No. 21-692 for branded tramadol extended-release tablets. Ortho-McNeil

currently markets Biovail's follow-on extended-release tablets under the brand name Ultram® ER.[4]

In January 2007, Par filed an ANDA with the FDA seeking approval to sell generic tramadol extended-release tablets based on data demonstrating bioequivalence to Biovail's Ultram® ER product. Pursuant to the Hatch-Waxman Act, Par certified that the '887 patent, which is listed in FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" ("the *Orange Book*") as covering Ultram® ER, is not infringed, invalid and/or unenforceable. Plaintiffs sued Par on May 9, 2007 alleging that the product described in Par's ANDA infringed the claims of the '887 patent. (D.I. 1). Plaintiffs subsequently amended their complaint to also include the '430 patent (D.I. 78), which is not listed in the *Orange Book* for Ultram® ER.

V. ARGUMENT

A. General Claim-Construction Principles

Because patent claims define the invention and delimit a patentee's right to exclude, a district court construes patent claims as a matter of law to determine their meaning and scope. *Markman v. Westview Instrs., Inc.*, 52 F.3d 967, 976, 980 (Fed. Cir. 1995) (en banc), *aff'd* 517 U.S. 370 (1996); *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1455 (Fed. Cir. 1998) (en banc).

In *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005), the Federal Circuit, sitting en banc, discussed claim-construction principles in detail and provided guidance for district courts to follow when construing claims. *Phillips* noted that there is no "magic formula" for conducting claim construction and instead identified a hierarchy for using intrinsic and extrinsic

[4] PriCara™, a unit of Ortho-McNeil, distributes Ultram® ER.

evidence to discern the meaning of claim language.[5] 415 F.3d at 1324. It said that "the claims themselves provide substantial guidance...." *Id.* at 1314. It then stated that a court may "rely heavily on the written description for guidance as to the meaning of the claims." *Id.* at 1317. It later indicated that the prosecution history may be "less useful" for claim-construction purposes than the written description. *Id.* It also explained that extrinsic evidence is "less significant than the intrinsic record for determining 'the legally operative meaning of claim language.'" *Id.* (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

A patent's claims define the invention and the patentee's right to exclude. *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004). Accordingly, a district court should look to the words of the claims themselves to ascertain the scope of the patented invention. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). And a court should generally assign claim language the ordinary and customary meaning it would have to a person of ordinary skill in the art at the time of the invention, i.e., as of the effective filing date of the patent application. *Phillips*, 415 F.3d at 1313; *see Housey Pharms., Inc. v. AstraZeneca UK Ltd.*, 366 F.3d 1348, 1352 (Fed. Cir. 2004).

Claim construction requires examination of the patent's written description. *Phonometrics, Inc. v. N. Telecom Inc.*, 133 F.3d 1459, 1464 (Fed. Cir. 1998). The ordinary meaning of claim language is the meaning it would have to those skilled in the art after reading

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[5] The intrinsic evidence consists of two components: the patent and its prosecution history. *Id.* at 1582. A patent contains two parts: first, the drawings (if any) and the text forming the patent's body, called the written description; second, the claims. The prosecution history—the rest of the intrinsic evidence—contains the record of the proceedings before the Patent Office and includes the prior art cited during examination and arguments, amendments and explanations made by the applicants to obtain allowance of the patent. *Phillips*, 415 F.3d at 1317; *Vitronics*, 90 F.3d at 1582. Extrinsic evidence consists of all evidence external to the patent and its prosecution history, such as dictionaries, treatises, inventor testimony, and expert testimony. *Markman*, 52 F.3d at 980.

the entire patent, including the written description. *Phillips*, 415 F.3d at 1313. While the written description should be considered, "it is improper to read limitations from the written description into a claim." *Wenger Mfg., Inc. v. Coating Mach. Sys., Inc.*, 239 F.3d 1225, 1237 (Fed. Cir. 2001).

A patentee may, however, act as a lexicographer by clearly setting forth in the written description an explicit definition for a claim term. *See, e.g., Jack Guttman, Inc. v. Kopykake Enters., Inc.*, 302 F.3d 1352, 1360 (Fed. Cir. 2002). But the patentee must demonstrate intent to deviate from a term's ordinary and customary meaning by expressing a different meaning in the written description "with reasonable clarity, deliberateness, and precision." *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1325, 1327 (Fed. Cir. 2002) (quoting *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994)). Vague or ambiguous statements in the written description do not suffice to alter a term's ordinary meaning. *W.E. Hall Co. v. Atlanta Corrugating, LLC*, 370 F.3d 1343, 1353 (Fed. Cir. 2004).

Claim construction also requires consideration of the patent's prosecution history. *Markman*, 52 F.3d at 980. Statements made by the applicant during prosecution in support of patentability may supply evidence of the meaning of disputed claim language. *See E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1438 (Fed. Cir. 1988).

A district court may consider extrinsic evidence to assist it in understanding scientific principles and the technology at the time of the invention. *See Markman*, 52 F.3d at 980. And a court may employ extrinsic evidence for claim construction purposes. *Phillips*, 415 F.3d at 1317. But a court should not use extrinsic evidence to vary or contradict the meaning of claim language where the intrinsic evidence determines the meaning. *Vitronics*, 90 F.3d at 1583-85.

Because dictionaries and treatises—although categorized as extrinsic evidence—provide insight into the ordinary and customary meaning of claim language, the Federal Circuit noted that they are "often useful" in claim interpretation. *Phillips*, 415 F.3d at 1322. In *Phillips*, the Federal Circuit confirmed that a district court may freely consult a dictionary "at any time" in order to understand the technology or construe claim language as long as the dictionary definition does not contradict the definition derived from the intrinsic evidence. *Id.*

Other extrinsic evidence, including an expert's opinion testimony, may also be useful to a court "to provide background on the technology at issue, to explain how an invention works, to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Phillips*, 415 F.3d at 1318. Thus, expert testimony that is consistent with the intrinsic record may assist the court in its claim construction.

B. The Meaning of the Disputed Terms in the '887 Patent and '430 Patent

The limitations in claim 1 of the '887 patent and claim 1 of the '430 patent are exemplary of the terms in dispute, each of which is bolded for emphasis below. (Colletti Decl. Ex. E-N).[6] Claim 1 of the '887 patent reads:

> 1. A controlled release oral pharmaceutical preparation suitable for dosing every 24 hours comprising
>
> a substrate comprising a **pharmaceutically effective amount of tramadol or a salt thereof**;
>
> said substrate coated with a controlled release coating;
>
> said preparation having a dissolution rate in vitro when measured using the Ph. Eur. Paddle Method at 100 rpm in 900 ml 0,1 N [sic 0.1 N] hydrochloric acid at 37° C. and using UV detection at 270 nm, between 0 and 50% tramadol released after 1 hour; between 0

[6] Exhibits referred to in this brief are attached to the accompanying Declaration of Robert E. Colletti, referred to as "Colletti Decl. Ex. __".

> and 75% tramadol released after 2 hours; between 3 and 95% tramadol released after 4 hours; between 10 and 100% tramadol released after 8 hours; between 20 and 100% tramadol released after 12 hours; between 30 and 100% tramadol released after 16 hours; between 50 and 100% tramadol released after 24 hours; and greater than 80% tramadol released after 36 hours, by weight, said preparation providing a **therapeutic effect for about 24 hours after oral administration**.

(Colletti Decl., Ex. A: '887 patent, claim 1 (emphasis added)). The only independent claim of the '430 patent, claim 1, reads:

> 1. A solid controlled release oral dosage form, comprising,
>
> a therapeutically effective amount of tramadol or a pharmaceutically acceptable salt thereof incorporated into a **normal release matrix**,
>
> said matrix overcoated with a controlled release coating comprising a polymethacrylate or a water insoluble cellulose,
>
> said dosage form providing a **therapeutic effect for at least about 24 hours**.

(Colletti Decl., Ex. B: '430 patent, claim 1 (emphasis added)).

1. The Term "Therapeutic Effect"

Par's Proposed Construction[7]	Plaintiffs' Proposed Construction[8]
The controlled release oral pharmaceutical preparation must produce analgesic efficacy in human patients experiencing pain as demonstrated by scientifically valid placebo-controlled clinical evidence.	Effective for the treatment of one or more clinical conditions, e.g., pain.

The term "therapeutic effect" is recited in asserted claims 1, 13 and 19 of the '887 patent, and claim 1 of the '430 patent.

[7] Colletti Decl. Ex. E.
[8] Colletti Decl. Ex. F.

b. "Therapeutic Effect For About 24 Hours" (i) Is a Separate and Distinct Limitation From "Suitable For Dosing Every 24 Hours and (ii) Requires Clinical Evidence From Human Patients

"[W]hen an applicant uses different terms in a claim it is permissible to infer that he intended his choice of different terms to reflect a differentiation in the meaning of those terms." *Innova*, 381 F.3d at 1119-20; *see also Bancorp Servs., L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1373 (Fed. Cir. 2004) (stating "the use of [two] terms in close proximity in the same claim gives rise to an inference that a different meaning should be assigned to each."). In the '887 patent, the phrase "suitable for dosing every 24 hours" is a separate and distinct recitation from the phrase "therapeutic effect for about 24 hours after oral administration." *Innova*, 381 F.3d at 1119-20; *Bancorp,* 359 F.3d at 1373. Otherwise, the use of the term "therapeutic effect for about 24 hours after oral administration" would be "unnecessary and superfluous" as the inventors could have easily used the phrase "suitable for dosing every 24 hours" alone. *Innova*, 381 F.3d at 1119; *see also Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 93 F.3d 1572, 1579 (Fed.Cir.1996) (stating that if two terms described a single element, "one would expect the claim to consistently refer to this element [with one or the other of the two terms], but not both, especially within the same clause").

As is consistent with their ordinary and customary meaning of these terms, the phrases "suitable for dosing every 24 hours" and "therapeutic effect for about 24 hours after oral administration" are not synonymous. The specification of the '887 patent and the '430 patent uses the phrases "suitable [or suited] for "once-a-day dosing" interchangeably with "suitable for dosing every 24 hours" and "twenty-four hourly[] administration" (Colletti Decl. Ex. A: '887 patent, *compare* col. 2, ll. 9-10, 24, col. 3, ll. 5-6 with claims 1, 13, 19 and with col. 1, l. 24).

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Thus, the phrase "suitable for dosing every 24 hours" has its ordinarily and customary meaning of "once-a-day dosing or administration."

Moreover, in an official proceeding, such as prosecution of a patent application with the U.S. Patent Office, a patentee has "every incentive to exercise care in characterizing the scope of its invention." *Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1350 (Fed. Cir. 2004). Here, the inventors of the '887 patent deliberately chose to distinguish the phrases "suitable for dosing every 24 hours" and "therapeutic effect for about 24 hours after oral administration."

"Therapeutic effect" is not expressly defined in the specification of the '887 patent or '430 patent, but the prosecution history of the '887 patent is informative. It makes perfectly clear that a "therapeutic effect for about 24 hours" (i) is a substantially different limitation from "suitable for dosing every 24 hours" and (ii) requires clinical evidence from human subjects. When the application that issued as the '887 patent was filed, the claims corresponding to the asserted claims in this case contained the limitation "suitable for dosing every 24 hours," but did not contain the limitation "therapeutic effect for about 24 hours." (Colletti Decl. Ex. A: '887 patent file history at PAR046199-PAR046206). The Patent Office rejected those claims. Among other rejections, the Patent Office found the claims anticipated and/or obvious over prior art. (Colletti Decl. Ex. C: '887 patent file history at PAR046316-PAR046320, PAR046348-PAR046351). To overcome the rejections, the applicants added the limitation "therapeutic effect for about 24 hours." (Colletti Decl. Ex. C: '887 patent file history at PAR04635, PAR046356-PAR046366).

And because the '430 patent shares the same specification with its parent, the '887 patent, Par's proposed construction for the phrase "therapeutic effect for about 24 hours after oral administration" in the '887 patent should be equally applied to the phrase "therapeutic effect for

at least about 24 hours" in the '430 patent. *Biovail Corp. Int'l v. Andrx Pharms., Inc.*, 239 F.3d 1297, 1301 (Fed. Cir. 2001) ("When multiple patents derive from the same initial application, the prosecution history regarding a claim limitation in any patent that has issued applies with equal force to subsequently issued patents that contain the same claim limitation.").

The plain meaning of once-a-day dosing or administration is clearly different than a "therapeutic effect for about 24 hours after oral administration." This is supported by the Declaration of Par's expert Dr. Weinberger. A drug suitable or approved for once-a-day dosing is not necessarily effective for the entire duration of a 24 hour period. (Weinberger Decl. ¶ 23). An approved dosing or administration regimen may be influenced by factors other than therapeutic effect, such as safety concerns, e.g., adverse events and/or toxicity. (Weinberger Decl. ¶ 23). Indeed, the prescribing information for Ultram® ER cautions against administering doses of tramadol exceeding 300 mg per day and one of the approved dosage strengths of Ultram® ER, 300 mg. (Colletti Decl. Ex. R at 3). Accordingly, as is consistent with their plain meanings, a pharmaceutical preparation that is suitable for dosing or administration once-a-day is separate and distinct from—and not necessarily— a pharmaceutical preparation that is effective for pain relief over the entire duration of a 24 hour period. (Weinberger Decl. ¶ 23).

Par's proposed construction is consistent with how the inventors used the phrase "therapeutic effect for about 24 hours after oral administration" during prosecution of the '430 patent. In distinguishing over prior art, the inventors stated that prior art formulations did not provide a therapeutic effect of tramadol "for a period of at least about 12 or about 24 hours as claimed," because it did not disclose data from clinical trials in human subjects:

> The Bondi reference does not teach, hint or suggest that the delivery systems described therein provide a therapeutic effect of the active agent for a **period of** at least about 12 or **about 24 hours** as claimed in independent claims 52 and 1, respectively. There are

> **no clinical trials reported therein**, there are **no indications that the dosage forms described therein were ever administered to human subjects**, and there is no teaching or suggestion of any desired pharmacokinetic parameters reported in Bondi. Therefore, a combination of the Raffa reference with the Bondi reference would not result in a dosage form which provides a therapeutic effect of the active agent for a **period of** at least about 12 or **about 24 hours**.

(Colletti Decl. Ex. D: '430 file history at PAR046780 (emphasis added)). These statements further demonstrate that the applicants defined the limitation "therapeutic effect for at least about 24 hours" as requiring clinical trials in human subjects.

Because the '430 patent is a continuation (child) of the '887 patent, and shares the same specification with the '887 patent (parent), the term "therapeutic effect" should be consistently applied between the two patents. *See Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1307 (Fed. Cir. 2007) (applying the same construction of a term used in related patents with the same specification); *see also Microsoft*, 357 F.3d at 1349-50.

The inventors' statements during the prosecution of the '887 patent and the '430 patent comport with Par's proposed construction and make clear that "therapeutic effect" (i) is separate and distinct from the claim language "suitable for dosing every 24 hours" and (ii) requires clinical evidence in human patients.

c. Par's Proposed Construction Is Supported By the Inventors and By One of Ordinary Skill

Relevant extrinsic evidence clarifies, and is fully consistent with, the intrinsic evidence demonstrating that the therapeutic effect is an analgesic effect demonstrated clinically with human patients to demonstrate a specific duration of the effect. This construction is supported, for example, by inventor Kevin J. Smith, Ph.D., who was the inventor responsible for clinical

pharmacology studies when the '887 and the '430 patents were filed.[11] At Dr. Smith's deposition, he testified that determining the efficacy of a pain-relief product requires a clinical study in human patients experiencing pain:

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Par's proposed construction is also supported by the testimony of

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can *in vivo* tests, such as pharmacokinetic tests, in healthy subjects who are not experiencing pain be used to determine analgesic efficacy:[12]

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Par's proposed construction is further supported by the Declaration of Dr. Weinberger, Par's expert. In Dr. Weinberger's opinion, the term "therapeutic" in the 1993-1994 timeframe means specifically "the treatment of disease." (Weinberger Decl. ¶ 14). And the term "therapeutic effect" as it relates to tramadol, a known analgesic agent, would be considered to mean that the product described by the claims causes an analgesic effect, which is "a reduced response to painful stimuli" or, for a patient with pain, a significant reduction in pain report or experience. (Weinberger Decl. ¶ 15).

Further, it is Dr. Weinberger's opinion that pain is a complex clinical symptom comprising various elements including both physical and psychological components. (Weinberger Decl. ¶ 16). Pain is detected and measured in a subjective manner. It is not possible to measure pain objectively as one can do with other clinical end-points, such as blood pressure. For example, pain measurements require a patient to indicate the magnitude and degree of pain on subjective scales that can rank from 0 (no pain) to 10 (worst possible pain) or categorical scales of 0 or no pain; 1, mild pain; 2, moderate pain; 3, severe pain. (Weinberger Decl. ¶ 17).

Several confounding variables can influence the reported efficacy of a given therapeutic intervention. The pain experience is often variable over time. The measurement of pain is inherently subjective and often difficult for the patient to quantify. The placebo response is often active, significant and can be profound. Therefore, to assess the efficacy of a single therapeutic intervention on the symptom of pain, it is routine to measure pain linearly over time in response to said intervention and compare this to placebo (Weinberger Decl. ¶ 18). As a result, one of ordinary skill would not interpret an analgesic response that was less than or equal to the response generated by a placebo as a therapeutic effect. (Weinberger Decl. ¶ 19). In other words, it is Dr. Weinberger's opinion that to be scientifically meaningful, a measured analgesic response must have statistical validity. (Weinberger Decl. ¶ 20).

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Accordingly,

Plaintiffs' proposed construction fails as it does not account for placebo-effects in human patients.

In sum, one of ordinary skill in the practice of pain medicine in the 1993-1994 timeframe would have interpreted "therapeutic effect" in the context of the '887 patent and the '430 patent to mean that the claimed controlled-release preparation must produce analgesic efficacy in human patients experiencing pain as demonstrated by scientifically valid, placebo-controlled evidence. (Weinberger Decl. ¶ 23).

2. The Phrases "Therapeutic Effect For At Least About 24 Hours" and "Therapeutic Effect For About 24 Hours After Oral Administration"

Par's Proposed Construction[14]	Plaintiffs' Proposed Construction[15]
The controlled release oral pharmaceutical preparation must produce analgesic efficacy in human patients experiencing pain as demonstrated by scientifically valid placebo-controlled clinical evidence and subsequent to oral administration of a dose of the preparation the analgesic efficacy in the patients must last for a period of about 24 hours from the time of onset of action.	Effective for the treatment of one or more clinical conditions, e.g., pain. (Plain and ordinary meaning; no construction necessary for "for at least about 24 hours" and "for about 24 hours after oral administration").

The phrase "therapeutic effect for at least about 24 hours" is recited in asserted claim 1 of the '430 patent. The phrase "therapeutic effect for about 24 hours after oral administration" is recited in asserted claims 1, 13 and 19 of the '887 patent. Each requires a specified duration of therapeutic effect, and Par's proposed construction is a plain meaning construction.

Moreover, Par's proposed definition is the ordinary and customary meaning as

[14] Colletti Decl. Ex. E.
[15] Colletti Decl. Ex. F.

determined from the perspective of a person of ordinary skill in the art at the relevant time.[16] One of ordinary skill would have understood that a once-a-day pharmaceutical preparation is not necessarily effective to relieve pain for the entire duration of a 24 hour period. (Weinberger Decl. ¶ 23). Such a person of ordinary skill would have understood that orally administered pharmaceutical preparations and, in particular controlled-release pharmaceutical preparations, do not necessarily act immediately upon ingestion and may take time to be absorbed prior to having a therapeutic effect. Accordingly, the therapeutic effect that is established in an appropriate clinical study would have been understood to have a duration beginning from the onset of the therapeutic effect for the specified time period of about 24 hours — and not a duration beginning from the time of dosing.

Par's proposed construction is also supported by Par's expert, Dr. Weinberger. In Dr. Weinberger's opinion, the duration of action for the pain medicine is measured from the onset of action—the time when the analgesic effect of the medicine separates from placebo to the time point when the medicine no longer separates from placebo. (Weinberger Decl. ¶ 22).

Accordingly, one of ordinary skill in the practice of pain medicine would have understood that a "therapeutic effect for about 24 hours" as it relates to orally administered tramadol is assessed for a duration of 24 hours from the time that pain relief begins, i.e., onset of action. (Weinberger Decl. ¶¶ 21-22).

[16] Par's proposed definition of the phrases "therapeutic effect for at least about 24 hours" and "therapeutic effect for about 24 hours after oral administration," which are based on their ordinary and customary meanings are also consistent with how the inventors used the term in the intrinsic record. (*See* Colletti Decl. Ex. D: '430 file history at PAR046780-PAR046791).

3. The Term "Matrix"

Par's Proposed Construction[17]	Plaintiffs' Proposed Construction[18]
A system wherein a drug is incorporated into a polymer(s) structure by either particle or molecular dispersion, wherein the former is a suspension of drug particles homogenously distributed in the polymer(s) structure and in the latter drug molecules are dissolved in the polymer, and wherein drug release occurs by diffusion through and/or erosion of the polymer structure.	A pharmaceutical preparation that incorporates the active ingredient dispersed within a solid dosage form.

The term "matrix" is recited only in the independent claim, claim 1, of the '430 patent, but not in the claims of the '887 patent.

Claim language should be assigned its ordinary and customary meaning as determined from the perspective of a person of ordinary skill in the art at the time of invention. *Housey*, 366 F.3d at 1352; *Phillips*, 415 F.3d at 1313. Par's proposed construction is taken from the Yihong Qiu and Guohua Zhang, *Research and Development Aspects of Oral Controlled-Release Dosage Forms*, in HANDBOOK OF PHARMACEUTICAL CONTROLLED RELEASE TECHNOLOGY, 465, 466-67 (Donald L. Wise ed., 2000). (Colletti Decl. Ex. S). Accordingly, Par's proposed construction is the ordinary and customary meaning of the term "matrix" as understood by one of ordinary skill in the art of controlled release pharmaceutical preparations at the time the '430 patent was filed.

A court may consider extrinsic evidence, such as a technical textbook, to determine the meaning of technical terminology to those of skill in the art at the time of the invention. *Phillips*, 415 F.3d at 1318. The extrinsic evidence should be considered in the context of the intrinsic evidence where applicable. *Id.* at 1321. Here, the intrinsic record is not informative as the term "matrix" is nowhere defined in the intrinsic record of the '887 patent or the '430 patent. The

[17] Colletti Decl. Ex. E.
[18] Colletti Decl. Ex. F.

specification merely provides examples of suitable materials for inclusion in a controlled release matrix. (Colletti Decl. Ex. A: '887 patent, col. 3, l. 52-col. 4, l. 25).

While the proposed constructions of both parties are similarly rooted in the concept of dispersion, Par's proposed construction clarifies this concept. In contrast, Plaintiffs' proposed construction is vague and ambiguous, failing to elucidate the term "dispersion." As a result, Plaintiff's proposed construction of "matrix" is redundant with the undisputed claim term "substrate." The parties have agreed that the term "substrate" means "a solid pharmaceutical preparation that contains the active ingredient." (Colletti Decl. Ex. G). Because Par's proposed construction properly distinguishes from other claim terms, it is the correct construction.

4. The Phrase "Normal Release Matrix"

Par's Proposed Construction[19]	Plaintiffs' Proposed Construction[20]
A matrix that does not slow the release of the active ingredient.	A matrix that does not substantially slow the release of the active ingredient.

The phrase "normal release matrix" is also recited only in the independent claim, claim 1, of the '430 patent, but not in the claims of the '887 patent. This phrase is nowhere defined in the intrinsic record of the '887 patent or the '430 patent.

The construction that aligns with the written description is the correct construction. *Phillips*, 415 F.3d 1303 at 1316. Par's proposed construction of the phrase "normal release matrix" faithfully adheres to the converse of the definition of a "controlled release preparation," *supra*, Sec. IV.A. A "controlled release preparation" is defined by the inventors in the specification as one that "achieves slow release of a drug." (Colletti Decl. Ex. B: '430 patent, col. 1, ll. 40-43). Plaintiffs' proposed construction is improper as it is contrary to the inventors'

[19] Colletti Decl. Ex. G.
[20] Colletti Decl. Ex. F.

definition of the phrase "controlled release preparation." It is not supported by the written description as it seeks to add the additional qualifying term "substantially" to describe "slow release." There is simply no support for the term "substantially" or the phrase "substantially slow" in the '887 patent and the '430 patent specification. Because Par's proposed construction aligns with the written description, it is the proper construction.

5. The Phrase "Pharmaceutically Effective Amount of Tramadol Or a Salt Thereof"

Par's Proposed Construction[21]	Plaintiffs' Proposed Construction[22]
An amount of tramadol or its salt contained in the substrate or the normal release matrix to achieve a therapeutic effect.	An amount of tramadol or its salt sufficient to provide at least some analgesia.

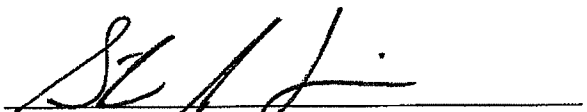
The phrase "pharmaceutically effective amount of tramadol or a salt thereof" is nowhere defined in the intrinsic record of the '887 patent or the '430 patent. This phrase is recited in the claims of the '887 patent, but not in the claims of the '430 patent. Claims 1, 13 and 19 of the '887 patent recite that a substrate or a tablet contain a "pharmaceutically effective" amount of tramadol or a salt thereof. (Colletti Decl. Ex. A). Claim 1 of the '430 patent instead recites the phrase "therapeutically effective amount of tramadol or a pharmaceutically acceptable salt thereof" in the context of a normal release matrix. (Colletti Decl. Ex. B: '430 patent, claim 1). The interchangeable use of the phrases "pharmaceutically effective" and "therapeutically effective" clearly demonstrates the inventors' understanding of these terms as being synonymous. *See Verizon*, 503 F.3d at 1307; *Microsoft*, 357 F.3d at 1349-50. Accordingly, Par's proposed construction utilizes the term "therapeutic effect."

[21] Colletti Decl. Ex. G.
[22] Colletti Decl. Ex. F.

The construction that stays true to the claim language is the correct construction. *Phillips*, 415 F.3d 1303 at 1316. Par's proposed construction comports with the intrinsic record and the inventors' own use of the phrase "pharmaceutically effective." In contrast, Plaintiffs' proposed construction is improper as it is contrary to the inventors' own claim language. In addition, it provides no further clarity as the phrase "some analgesia" is vague and ambiguous. Because Par's proposed construction aligns with analogous claim language, it is the proper construction.

VI. CONCLUSION

For the foregoing reasons, Par respectfully requests that the Court enter an order construing the terms and phrases of the '887 patent and the '430 patent as proposed by Par.



Frederick L. Cottrell, III (#2555)
Cottrell@rlf.com
Steven J. Fineman (#4025)
Fineman@rlf.com
Richards, Layton & Finger P.A.
One Rodney Square
P.O. Box 551
Wilmington, DE 19899
(302) 651-7700
Attorneys for Defendants Par Pharmaceutical, Inc. and Par Pharmaceutical Companies, Inc.

Of Counsel

Edgar H. Haug
Robert E. Colletti
Jonathan R. Wise
Angus Chen
Frommer Lawrence & Haug LLP
745 Fifth Avenue
New York, NY 10151
(212) 588-0800

Dated: June 13, 2008

IN THE UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

I hereby certify that on June 13, 2008, I electronically filed the foregoing document with the Clerk of Court using CM/ECF which will send notification of such filing(s) and Hand Delivered to the following:

Jack B. Blumenfeld, Esquire
Rodger D. Smith II, Esquire
Morris, Nichols, Arsht & Tunnell LLP
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899-1347

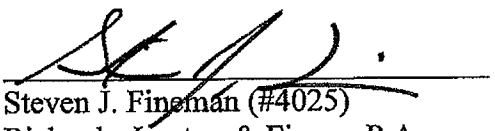
Richard D. Kirk, Esquire
The Bayard Firm
222 Delaware Avenue, Suite 900
P.O. Box 25130
Wilmington, DE 19899-5130

Mary W. Bourke, Esquire
Conolly Bove Lodge & Hutz LLP
The Nemours Building
1007 North Orange Street
P.O. Box 2207
Wilmington, DE 19899

I hereby certify that on June 13, 2008, I have sent by Electronic Mail, the foregoing document to the following non-registered participants:

Robert J. Goldman, Esquire
Ropes & Gray LLP
525 University Avenue
Suite 300
Palo Alto, California 94310

Richard A. Inz
Sona De
Ropes & Gray LLP
1211 Avenue of the Americas
New York, New York 10036



Steven J. Fineman (#4025)
Richards, Layton & Finger, P.A.
One Rodney Square
P.O. Box 551
Wilmington, Delaware 19899
(302) 651-7700
fineman@rlf.com

CERTIFICATE OF SERVICE

I hereby certify that on June 24, 2008, true and correct copies of the foregoing were caused to be served on counsel of record at the following addresses as indicated:

BY HAND DELIVERY
Jack B. Blumenfeld, Esquire
Rodger D. Smith II, Esquire
Morris, Nichols, Arsht & Tunnell LLP
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899-1347

BY HAND DELIVERY
Richard D. Kirk, Esquire
The Bayard Firm
222 Delaware Avenue, Suite 900
P.O. Box 25130
Wilmington, DE 19899-5130

BY HAND DELIVERY
Mary W. Bourke, Esquire
Conolly Bove Lodge & Hutz LLP
The Nemours Building
1007 North Orange Street
P.O. Box 2207
Wilmington, DE 19899

BY ELECTRONIC MAIL
Robert J. Goldman, Esquire
Ropes & Gray LLP
525 University Avenue
Suite 300
Palo Alto, California 94310

BY ELECTRONIC MAIL
Richard A. Inz, Esquire
Sona De, Esquire
Ropes & Gray LLP
1211 Avenue of the Americas
New York, New York 10036

Frederick L. Cottrell, III (#2555)